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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,499	05/04/2001	Herman Waldmann	1324.028	8699

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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,499	WALDMANN ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 23 May 2006.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 64,68-95,105-108,110 and 111 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 64,68-95,105-108,110 and 111 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/23/06 has been entered.

Applicants' amendment and Response, filed 5/23/06 and 2/23/06 have been considered and entered. The Amendment filed 5/23/06 is responsive to the Notice of Non-Compliant Amendment, mailed 4/24/06.

Claims 64, 70, 95, 110 are amended; claims 64, 68-95, 105-108, 110 and 111 are pending and under current examination.

Claim Objections

The prior objection of claim 110 is withdrawn in view of Applicants' amendment to the claim.

Specification

The prior objection to the specification is maintained. Applicants have submitted a replacement specification that comprises the text of the parent published PCT reformatted in accordance with current USPTO practice. However, the substitute specification filed 2/12/03 and 11/23/05 has not been entered because it does not conform to 37 CFR 1.125(b) because: Applicants have not provided a copy of the specification excluding the claims, as well as a marked up version of the specification showing all the changes (including the matter being added to and the matter being deleted from) to the specification of record. See also MPEP §608.01(q).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claims 64, 68-95, 105-108, 110 and 111 is *maintained* under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for producing a long-term culture of immature dendritic cells wherein the method comprises culturing mouse or human ES cells *in vitro* in the presence of IL-3 [and optionally, murine GM-CSF] to bring about differentiation of the ES cells into immature dendritic cells and stimulating the maturation of the immature dendritic cells.

The specification does not reasonably provide enablement for methods for producing long-term cultures of immature dendritic cells by culturing the ES cells in the presence of any cytokine or combination of cytokines to bring about the differentiation of the ES cells into immature dendritic cells to produce a long-term culture of immature dendritic cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is maintained for reasons of record, advance in the Office action mailed 8/23/05.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Applicants' assert that the now-amended claims reciting mouse or human ES cells, obviates the prior enablement rejection. See page 9 of the Response, filed 5/23/06.

These arguments are considered, but not found to be persuasive. Applicants' amendments do not enable the claims. Firstly, the preamble of claim 64, now recites the production of "mouse or human" dendritic cells. However, the method steps of claim 64 do not require using mouse/human ES cells in order to produce the mouse/human dendritic cells. The specification fails to provide specific guidance (culture conditions, starting materials, etc.) with regard to using non-mouse ES cells to produce immature mouse dendritic cells. Similarly, the specification does not teach using non-human ES cells to produce immature human dendritic cells. Applicants should consider drafting the claims such that one set read upon production of immature human dendritic cells using human ES cells, and the other set directed to production of immature mouse dendritic cells using mouse ES cells.

The specification provides a single working example, by culturing the ESF116 mouse cell line with a particular cytokine, murine IL-3. The state of the art of directing differentiation of ES cells to a particular cell type is found to be unpredictable, the working example shows that using different combinations of cytokines, only GM-CSF and IL-3 have found to have the capacity to support DC development. As stated in prior Office actions, and stated by Applicants, that the breadth of "any cytokine" does not enable the claimed invention, because Applicants have found that only IL-3 is capable of producing immature dendritic cells, as required by the claims. See also, page 6 of the Office action, mailed 4/9/03 and Applicants' Response, 2/12/03, p. 8, 2nd full ¶. Furthermore, one of skill in the art could not rely upon the state of the art of utilizing any cytokine for the claimed methods, because cytokines have varying biological functions. For example, Abbas and Lichtman (*Cellular and Molecular Immunology*, Philadelphia, P.A., Elsevier Saunders, 1991, p. 249) provide Table 11-3, which shows that cytokines have

different cell targets and biological effects. For example, TNF (tumor necrosis factor) has a principal cell source of macrophages, T cells, and is involved in inflammation, apoptosis; chemokines (which include a wide variety of cytokines) have different cell sources, have a cell target of leukocytes, and different biological effects, such as chemotaxis and activation. Thus, the term "cytokine" encompasses a large family of polypeptides that have varied biological functions. One of skill in the art could not predictably use any cytokine, as broadly claimed, in order to practice the claimed invention. Furthermore, it would have required undue experimentation, given the diversity of function and large number of family members that are considered cytokines, to determine which cytokine would bring about differentiation of ES cells into immature dendritic cells, as required by the claim. The specification only provides guidance for IL-3, and optionally GM-CSF, with regard to the claimed invention. IL-3 is found to be a critical element that is required to enable the claimed invention. Thus, the breadth of the claims, encompassing any cytokine, or combination thereof, is not found to be enabled.

Accordingly, in view of the quantity of experimentation necessary for the production of long-term cultures of immature dendritic cells by culturing any ES cells with any cytokine [or combination thereof], the lack of guidance, teachings and examples provided by the specification for the production of long-term cultures of immature dendritic cells from any ES cells with any cytokine, other than the mouse or human ES cell lines with IL-3 [and optionally murine GM-CSF, and the requirement for IL-3 for differentiation, it would have required undue experimentation for one skilled in the art to make and/or use the claimed long-term cultures of dendritic cells and methods of making the same.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 81-83 and 90 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 81 recites the limitation "the gene" in line 1. There is insufficient antecedent basis for this limitation in the claim. The claim depends from either claims 78 or 79. The term "the gene" lacks antecedent basis with regard to claim 78, because the cell must express two or more genes.

Claim 82, as written, is unclear. The claim recites the process of claim 64, wherein one or more endogenous gene(s) have been inactivated. The metes and bounds of this claim are unclear, because it is not clear what cell has an inactivated endogenous gene(s), the ES cell, or the immature dendritic cell. Claim 83 depends from claim 82.

Claim 90 is unclear. The claim recites that the recovered cell is "substantially pure". It is unclear what "substantially pure" encompasses in this limitation. The recovery of a cell (as recited by the claim) would be considered only cell type, because the recovered cell is a single cell. It is unclear how a single cell could not be "substantially pure".

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Ram Shukla, SPE of Art Unit 1632, at (571) 272-0735. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

thaian ton

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